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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,445	11/16/2001	Ernest G. Schutt	ALLIA.62F1C1C1	3983

48394 7590 01/12/2006

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EXAMINER	
SHARAREH, SHAHNAM J	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,445	SCHUTT ET AL.	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/18/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment filed on October 24, 2005 has been entered. Claims 1-10, 12-20 are pending. Applicant has made an election of species on the Paper filed on July 2003. Accordingly, perfluorobutane was elected as the species for fluorocarbons and oxygen was elected as the species for the modifier gas. Claims 1-10, 12-20 read on the elected species and are pending.

Applicant's arguments filed on December 28, 2004 have been fully considered but are now moot in view of new grounds of rejection. Any rejection that is not addressed in this Office Action is considered obviated in view of the amendment.

Double Patenting

1. Claims 1-10, 12-20 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of 1-12 of US Patent 6,372,195, claims 1-101 of US Patent 6,258,339, claims1-24 of US Patent 5,695,741, claims 1-38 of US Patent 5,639,443, and claims 17-22 of US Patent 5,798,091, claims 1-9, 38-73 of US Patent 5,804,162, claims 26-51 of US Patent 6,193,952 for the reasons or record

Applicant's request to revisit this rejection after the claims have been formally allowed is noted.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 1-10, 13-18, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider et al US Patent 5,413,774.

The instant claims are directed microbubbles comprising at least one fluorocarbon gas and at least one modifier gas that can comprise oxygen. The scope of the instant limitation "modifier gas" is described in paragraphs 0034, 0061-0069. Accordingly, the scope of the term "a modifier gas" is inclusive and encompasses other gases such as oxygen, air, perfluorocyclooctane, perfluoropentane, perfluoroethane and perfluoromethane. The instant claims further require a ratio of the modifier gas to the fluorocarbon gas in the ranges of 1:100 to about 1000:1.

Schneider meets the limitations of the claimed microbubbles. Schneider teaches gas filled microvesicles that can contain a mixture of a first perfluorocarbon gas such as perflorobutane (C4F10) and a secondary gas such as air which contains oxygen, nitrogen, CO2. (see col 5, lines 50-56., examples 7-8*, claims 1-2, col 14, lines 45, 68). The second gas of Schneider can include other perfluorocarbons such as perfluoromethane or perfluorethane. (see (col 14, lines 42-49). Schneider also teaches a membrane around his microvesicles (see claims 5-9). Schneider's fluorocarbon is the same as those instantly claimed; therefore, it possesses the same functional characteristics as the instant fluorocarbon.

Air, nitrogen and the like gases including other perfuorocarbons also fall within the instant genus of modifier gases. Thus, the microbubbles of Schneider contains a perfulorobutane. The microbubbles of Schneider also comprise a secondary gas including air, perfluormethane, which meets the instant limitation "modifier gas."

Schneider's microbubbles comprise a membrane comprising phospholipids or albumin. (see col 13-14). Scheider administers his microvesicles to Rabbits thus exposing them to an external medium comprising blood and other physiological gases such as air or oxygen. (see examples 2-4, cols 9-11). Thus, Schneider meets all structural limitations of the instant claims and all functional limitations of the instant claims. Schneider only fails to specifically recite the instantly claimed ranges of modifier gas to fluorocarbon gas.

However, absent a showing of unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize the concentrations of individual gases in Schneider's microbubbles by routine experimentation to observe the most effective clinical results.

3. Claims 12, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider et al US Patent 5,413,774 in view of Tickner US Patent 4,265,251.

The teachings of Schneider are described above. Schneider only fails to incorporate delivery of oxygen in his microbubbles.

Tickner teaches methods of ultrasound imaging using gas containing microbubbles wherein the gas is oxygen (abstract, col 7, lines 11-54). Tickner teaches that although the preferred gas is carbon dioxide, however, other gases such as freons and oxygen may be used in his contrast agents (col 6, lines 63-67)..

Although Schneider fails to use oxygen with pefluorobutane in his gaseous mixtures compositions, he specifically teaches that any gas like air and nitrogen can be employed in his gaseous mixture. Tickner shows that for the purposes of ultrasonic

contrast agents, gases such as oxygen, nitrogen, and Freons are substantially interchangeable and are functional equivalents.

Thus, absence of showing unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to substitute one of air or nitrogen gases in Schneider's microvesicles with oxygen and create a microvesicle that contains pefluorobutane and oxygen, because as shown by Tickner, oxygen is considered art recognized equivalents to suitable gases enumerated by Schneider. Subsequently, the ordinary skill in the art would have had a reasonable expectation of success in mixing perfluorobutane with oxygen to produce a gaseous microvesicles.

4. Claims 1-10, 12-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider in view of Clark US Patent 5,536,753.

The teachings of Schneider are described above. Schneider does not specifically uses oxygen in his gaseous mixture.

Clark is used to show that perflourocarbon containing emulsions are safe oxygen transport agents. (see abstract). Clark also teaches the use of emulsifying agents such as phospholipids and polymeric agents that can entrap the gas within his formulation (see col 2, lines 43-55). Clark further employs such fluorocarbons as perfluoromethylcyclohexanes that fall within the scope of the instantly claimed perfluorocyclohexanes (see col 2, lines 39 and col 4, lines 60-64). Clark further elaborates on suitable concentrations of perfluorocarbon, the surfactant and the oxygen (see col 3-4; specifically col 3, lines 23-65).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to utilize a mixture of a perfluorocarbon with oxygen, because as suggested by Schneider and Clark, the ordinary skill in the art would have had a reasonable expectation of success in preparing microbubble for in vivo delivery of oxygen. Absence of showing unexpected results, one of ordinary skill in the art would have had a reasonable expectation of success for optimizing the concentrations of perfluorocarbon and oxygen for effective clinical or diagnostic use, when mixing the perfluorocarbon with oxygen.

Conclusion

No claims are allowed.

The Office Action is made final because either Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action or the new ground of rejection was prompted by a prior art included in Applicant's submitted information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p). Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a) and MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 571-272-0630. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER